

The incomplete papillotomy: when less is worse

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Abstract

Bleeding after endoscopic retrograde cholangiopancreatography occurs in around 2% of cases, with only a minority of cases being severe. Several independent risk factors have been established including anticoagulant intake, low platelet count, cirrhosis, dialysis for end-stage renal disease, intraprocedural bleeding, and low endoscopist experience. The aim of our study was to evaluate whether the length of papillotomy influences bleeding rates. 403 patients have been prospectively monitored over an 8 months period in a tertiary center in Romania. The overall incidence of bleeding was 2.98%. Incomplete papillotomy was significantly associated with a higher risk of bleeding in both univariate (5.33%, $\chi^2=7.43$, 95%CI, $P=.024$) and multivariate (OR=3.97, 95%CI: 1.122-4.086, $P=.032$) analyses. Such results may add to the current status quo of endoscopic sphincterotomy and may be explained by distribution of coagulation current alongside the incision. Moreover, undercutting may contribute to intraprocedural device related trauma. Therefore, results should be interpreted with caution but the length of papillary incision should be evaluated by subsequent large volume studies.

Keywords: post-ERCP bleeding, risk factor, adverse event, ERCP

Introduction

First universally accepted post-endoscopic retrograde cholangiopancreatography (ERCP) adverse events classification was performed by Freeman et al. in a landmark prospective study of 2347 patients undergoing ERCP where overt bleeding occurred in 2% of patients, with 0.5% of patients experiencing severe bleeding [1]. Ever since, that study, papillotomy has been referred to as a maneuver with an increased risk for bleeding. As a post-ERCP adverse event, bleeding is in most cases caused by biliary and/or pancreatic papillotomy. However, post-procedural bleeding can be triggered by vessel injury, pseudoaneurysms, splenic, hepatic or duodenal injuries, being considered to have a cumulated incidence of up to 2% of cases undergoing ERCP [1-3]. Nevertheless, reported numbers highly vary depending on definitions and follow-up protocols. A relatively particular situation is that of post-procedural hemobilia which can occur also as a late-onset complication mainly due to dilation of strictures or intraductal ablative procedures [3, 4].

In what the intra-procedural papillotomy (or endoscopic sphincterotomy) maneuver is concerned, anatomical dissection studies state that the recommended papillary incision area is the one between 10 and 11 o'clock, as it hosts only approximately 10% of all papillary arteries [5]. Such finding, although valuable, isn't universally accepted as major bleeding can occur despite following such recommendation. With regard to the electrosurgical method recommended for incision, it has been considered that blended current, in opposition to pure cutting current, should be used

in all patients as it reduces the incidence of bleeding without significantly increasing the risk of PEP due to thermal injury of the coagulation phase [6, 7]. In this respect a relatively large scale meta-analysis conducted on 3 randomized controlled trials gathering 594 patients exposed to ERCP and papillotomy concluded that bleeding rates dropped when EndoCut (Erbe, Tübingen, Germany) was used compared to other blended current but such assumption should be interpreted with caution due to the wide use of the Erbe-developed EndoCut module in tertiary clinics globally [8].

There is a multitude of reliable studies that have investigated risk and causality for post-ERCP bleeding establishing a series of independent risk factors for bleeding like anticoagulant intake, platelet count under 50000/mm³, cirrhosis, dialysis for end-stage renal disease, intraprocedural bleeding, and low endoscopist experience [9].

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Given the fact that to date it has not been explored how the length of the intraduodenal portion of the common bile duct influences sphincterotomy, the aim of our study was to evaluate whether such complete or incomplete papillotomy influences the overall risk for bleeding.

Methods

Patients

We have prospectively monitored patients referred for therapeutic ERCP within the Institute of Gastroenterology and Hepatology of Iasi, an emergency-based tertiary center in Romania, between the 1st of January and the 31st of August 2018.

All patients were managed for both malignant and benign bile duct disease. Inclusion criteria consisted in: (i) indication for ERCP: bile duct stones (including cholangitis and biliary pancreatitis), cholangiocarcinoma, pancreatic cancer and chronic pancreatitis, bile duct injuries, various extrinsic compressions, primary sclerosing cholangitis, and post-liver transplantation strictures; (ii) age above 18 years old; (iii) possibility for follow-up 15 to 60 days; (iv) expressed consent for inclusion in the study. Exclusion criteria were: (i) postoperative altered anatomy; (ii) duodenal and/or bilio-pancreatic trauma; (iii) cannulation of the minor papilla; and (iv) impossibility for achieving cannulation. Data regarding patient demographics and ERCP indication have been recorded in all cases.

Classification of papillotomy and procedure documentation

During all ERCP procedures the duodenoscope was advanced to the papillary region. Guidewire-assisted technique was used for primary biliary cannulation using Single-use triple lumen sphincterotomes Olympus CleverCut3V, with 25mm cutting wire. Needle-knife freehand precut or fistulotomy were performed using Olympus NeedleCut3V 5mm Needle Knife sphincterotomes. Sphincteroplasty was performed using Endoflex Biliary Multi-Stage Dilation Balloons (different sizes). Video documentation of the ERCP procedure was performed in all cases. Bile duct cannulation was monitored. The need for freehand precut sphincterotomy, fistulotomy or transpancreatic septotomy was separately documented.

ERCP procedures have been performed by two experienced endoscopists (with an over 1000 ERCPs experience) and two senior fellows in advanced endoscopy (with an over 180 ERCPs experience). Free hand needle knife sphincterotomy (from the orifice), needle knife fistulotomy (above the orifice) have been performed as decided by the endoscopist only in cases with difficult standard cannulation. Transpancreatic biliary sphincterotomy has been considered after the second unintentional pancreatic duct cannulation. Mixed electrosurgical current was used in all cases for papillotomy (ERBE ICC200 electrosurgical device). Complete biliary sphincterotomy and partial (incomplete) papillotomy were recorded, decision was taken by the case-endoscopist.

Papillotomy was classified as complete when both ampullary and biliary sphincters were cut to the maximal length of the intraduodenal choledochal visible length. As shown in Figure 1, the common bile duct visible length with an *en face* papilla is correspondent to the ampullary and biliary

sphincters. All papillotomies which did not reach the maximal choledochal length were classified as incomplete. Not all patients received papillotomy. Data regarding the methods used for cannulation, brush cytology or balloon sphincteroplasty were recorded for univariate analysis, ROC curve analysis and multiple regression.

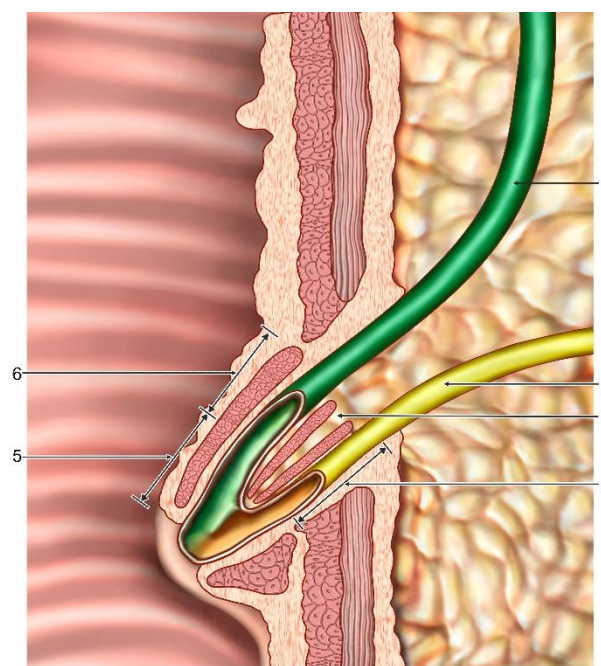


Figure 1. Anatomy of the papilla: 1. Common bile duct; 2. Pancreatic duct;

3. Septum: mixed muscle fibers; 4. Pancreatic sphincter; 5. Ampullary sphincter; 6. Biliary sphincter (adapted after Cotton et al., 2019) [2].

Prospective evaluation

All patients were hospitalized at least 24 hours after ERCP. Thorough clinical assessment together a biochemical panel including complete cell count, have been performed in all patients at least 24 hours after ERCP. Discharge was decided only at decision of the consultant. Further hospitalization and monitoring of patients was performed depending on the presence of post-ERCP complication or on the overall recovery of patients. All patients were prospectively followed up at 15 and 60 days. Adverse events including post-ERCP pancreatitis, bleeding, infection and perforation were defined according to consensus criteria of the American Society of Gastrointestinal Endoscopy (ASGE) [3]. Definition of post-ERCP pancreatitis was done after the revised Atlanta classification criteria. Post-procedural mortality was recorded.

Statistical analysis

Statistical analyses and calculations were made with the SPSS version 25 (IBM, Armonk, NY). Numerical data was reported as mean values and standard deviation. Comparisons within the analyzed groups were performed with Yates Chi-square test for categorical data. The prediction power of

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variables has been obtained using receiver operating characteristic (ROC) curves and calculating the area under the curve (AUROC). Categorical variables were presented in absolute (n), or relative (%) numbers. We searched for possible predictors of each post-ERCP adverse event and of the cumulative complications rate. Besides the extent of papillotomy, univariate analysis has been conducted also for other intraprocedural variables possibly influencing bleeding rates. Univariate analysis of predictors and multivariate analysis were done after the logistic regression model. Odds ratio (OR) has been calculated. Marked effects of tests were considered significant at $P < .05$.

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the

Grigore T. Popa University of Medicine and Pharmacy of Iasi, Romania.

Results

403 patients were included in the study and prospectively monitored. Only clinically significant post-procedural hemorrhages were reported as adverse events. Post-ERCP bleeding had an overall incidence of 2.98% of cases, with 1% mild bleeding, 1.5% moderate bleeding and 0.5% severe cases. Almost 1.5% of patient required transfusion of blood with a mean number of 2 transfused units per patient. On the other hand, up to 7% of patients showed non-clinically significant intra-procedural papillary bleedings which was either self limited or managed by submucosal epinephrine 1/20.000 injection according to local protocol. Risk factors for bleeding were assessed by univariate analysis as shown in Table 1.

Table 1. Univariate analysis of intraprocedural ERCP maneuvers for assessment of the risk of bleeding

ERCP maneuver	Post-ERCP bleeding		Test#	Correlation (r)	P-value (95%CI)
	Absent (n=391)	Present (n=12)			
Papillotomy					
No papillotomy	91 (100%)	0 (0%)	7.4393	.2756	.0242*
Incomplete	127 (94.78%)	7 (5.22%)			
Complete	173 (97.19%)	5 (2.81%)			
Freehand needle-knife	24 (96.%)	1 (4.%)	1.4628	.3154	.6908
Fistulotomy	4 (100%)	0 (0%)			
Transpancreatic biliary sphincterotomy	9 (90%)	1 (10%)			
Brush cytology Benign/Malignant	379/12 (97.18%/92.31%)	11/1 (2.82%/7.69%)	.0350	.4833	.03514*
Sphincteroplasty No/Yes	314/77 (96.62%/98.72%)	11/1 (3.38%/1.28%)	.3723	-.4590	.0417*

Yates Chi-square test

(*) Marked effects are significant at $P < .05$

Univariate analysis demonstrated that incomplete papillotomy was significantly associated with a higher risk of bleeding (5.33%, $\chi^2=7.43$, 95%CI, $P=.024$) when compared to complete papillotomy (2.81%) or to absence of papillotomy (no cases of bleeding). Alternative rescue papillotomy techniques did not significantly influence the overall risk of bleeding nevertheless bleeding was encountered in 10% of

transpancreatic access biliary sphincterotomies when compared to 4% of freehand needle-knife precut papillotomy or 0% of precut fistulotomy cases ($\chi^2=1.46$, 95%CI, $P=.690$). Brush cytology slightly increased the risk for bleeding in malignant strictures to 7.79% ($\chi^2=.03$, 95%CI, $P=.035$) and the use of balloon sphincteroplasty significantly lowered the bleeding rates to 1.28% ($\chi^2=.372$, 95%CI, $P=.041$).

Table 2. Prediction model for intraprocedural ERCP maneuvers associated with the risk of bleeding

ERCP maneuver	Area under ROC curve (AUC)	Standard Error ^a	P value ^b	AUC 95% CI	
				Min.	Max.
Incomplete papillotomy	.667	.050	<.0001	.569	.765
Brush cytology - malignant	.613	.042	.018	.531	.694
Absence of sphincteroplasty	.616	.050	.015	.518	.715

a. Under the nonparametric assumption ; b. Null hypothesis: true area = 0.5

Given the univariate correlations, power of prediction for the significant associations was performed by ROC curve analysis. Thus, we found that incomplete papillotomy significantly predicts post-procedural bleeding (AUC=.667, 95%CI: .569-.765, P<.0001). Moreover, an increased risk for post-ERCP bleeding is also predicted by the presence of malignant strictures and brush cytology (AUC=.613, 95%CI: .531-.694, P=.018) and by the absence of balloon sphincteroplasty (AUC=.616, 95%CI: .518-.715, P=.015). The

predictors are also independent risk factors for bleeding as confirmed by multiple regression (Table 3). Incomplete papillotomy increases risk for post-ERCP bleeding (OR=3.97, 95%CI: 1.122-4.086, P=.032). However, a greater risk seems to be triggered by presence of malignant strictures (OR=6.59, 95%CI: 1.56-7.84, P=.01). The sole use of sphincterotomy in absence of sphincteroplasty, although less significant, is also an independent risk factor for bleeding according to multiple regression (OR=.279, 95%CI: .181-.961, P=.043).

Table 3. Multivariate analysis of predictors

Multiple regression	SE	P value	Odd ratio Exp(β)	95% CI for Exp(B)	
				Lower	Upper
Incomplete papillotomy	.645	.032	3.976	1.122	4.086
Brush cytology - malignant	.735	.010	6.592	1.560	7.845
Absence of sphincteroplasty	.630	.043	.279	.181	.961
Constant	.635	.000	.019		

CI – confidence interval, SE-standard error

() Marked effects are significant at p < .05*

Discussion

Overall incidence of post-ERCP bleeding in the prospectively monitored cohort is comparable to that reported within practice guidelines [3,9]. The findings reported in univariate analysis show that the length of incision seems to influence the risk of bleeding, a partial sphincterotomy being associated with a higher risk for post-procedural hemorrhage. Quality of such evidence is supported also by ROC curve analysis and multiple regression. Possible rationale for such a

finding can be either dependent to the local spread of electrosurgical current or to the possible increased intraprocedural trauma in a partially dissected papilla. It has been shown that the type of current used for ES seems to affect the risk of bleeding [3], a relatively recent meta-analysis reporting that coagulation current significantly decreases the risk of bleeding [7]. The length of dissection is clearly proportional to the tissue exposure to coagulation current and thus, a longer exposure could prevent bleeding. Other subsequent studies raise the same question [7,10,11].

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Another debated issue related to the pattern and length of incision is that of the relationship between precutting and bleeding. Its role is considered controversial [9]. The results of our study are sustained by two meta-analyses gathering 13 randomized controlled trials and over 2000 patients showing that early precut sphincterotomy in difficult biliary access did not increase the rate of post-ERCP bleeding [12, 13]. Consequently, our study showed that absence of balloon dilation could increase the overall risk for bleeding. Such finding should be interpreted mainly for cases where a larger biliary access is needed for extraction of difficult biliary stones, where endoscopic sphincterotomy associated with balloon dilation is unanimously recommended [3,9,14]. Hemorrhagic post-ERCP complications were less frequent when sphincteroplasty was added to ES, compared to ES alone [15, 16]. Nevertheless, there are studies reporting the contrary [17,18]. Thus, the extent of sphincterotomy has been reported as significant [19].

Not the least, hemobilia should be reported as a different type of hemorrhagic adverse event of ERCP because of the different pathogenic pattern. Therefore, brush cytology within malignant strictures should not itself be seen as a risk factor for bleeding but as a procedure encountered in patient with an increased risk for hemobilia. The same should be stated also for hemosuccus pancreaticus. To what extent such manifestations are iatrogenic or pure consequences of malignancy is still a debated issue [20]. Proper follow-up and prompt diagnosis of such patients are otherwise mandatory for all ERCP endoscopists.

Conclusion

Although rare, post-ERCP bleeding is one of the major procedural adverse events that may need emergent action, reintervention or advanced interventional hemostasis. Proper training for identification of anatomical landmarks prior to papillotomy is mandatory. Length of incision seems to influence post-procedural outcomes, nevertheless further studies are required for validation. To what extent the low endoscopist experience influences the pattern of incision subsequently generating additional risk is also an important cofactor to be debated.

Conflict of Interest

Authors have no conflict of interest to disclose

References

1. Freeman ML, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ, Moore JP, Fennerty MB, Ryan ME, Shaw MJ, Lande JD. Complications of endoscopic biliary sphincterotomy. *New England Journal of Medicine*. 1996 Sep 26;335(13):909-19.
2. Cotton PB, Garrow DA, Gallagher J, Romagnuolo J. Risk factors for complications after ERCP: a multivariate analysis of 11,497 procedures over 12 years. *Gastrointestinal endoscopy*. 2009 Jul 1;70(1):80-8.
3. Chandrasekhara V, Khashab MA, Muthusamy VR, Acosta RD, Agrawal D, Bruining DH, Eloubeidi MA, Fanelli RD, Faulx AL, Gurudu SR, Kothari S. Adverse events associated with ERCP. *Gastrointestinal endoscopy*. 2017 Jan 1;85(1):32-47.
4. Wolters F, Ryan B, Beets-Tan R, Dejong C. Delayed massive hemobilia after biliary stenting. *Endoscopy*. 2003 Nov;35(11):976-7.
5. Mirjalili SA, Stringer MD. The arterial supply of the major duodenal papilla and its relevance to endoscopic sphincterotomy. *Endoscopy*. 2011 Apr;43(04):307-11.
6. Rey JF, Beilenhoff U, Neumann CS, Dumonceau JM. European Society of Gastrointestinal Endoscopy (ESGE) guideline: the use of electrosurgical units. *Endoscopy*. 2010 Sep;42(09):764-72.
7. Verma D, Kapadia A, Adler DG. Pure versus mixed electrosurgical current for endoscopic biliary sphincterotomy: a meta-analysis of adverse outcomes. *Gastrointestinal endoscopy*. 2007 Aug 1;66(2):283-90.
8. Li DF, Yang MF, Chang X, Wang NN, Tan FF, Xie HN, Fang X, Wang SL, Fan W, Wang JY, Yu ZC. Endocut versus conventional blended electrosurgical current for endoscopic biliary sphincterotomy: a meta-analysis of complications. *Digestive diseases and sciences*. 2019 Feb 18:1-7.
9. Dumonceau JM, Kapral C, Aabakken L, Papanikolaou IS, Tringali A, Vanbiervliet G, Beyna T, Dinis-Ribeiro M, Hritz I, Mariani A, Paspatis G. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2020 Feb;52(02):127-49.
10. Kohler A, Maier M, Benz C, Martin WR, Farin G, Riemann JF. A new HF current generator with automatically controlled system (Endocut mode) for endoscopic sphincterotomy-preliminary experience. *Endoscopy*. 1998 May;30(04):351-5.
11. Perini RF, Sadurski R, Cotton PB, Patel RS, Hawes RH, Cunningham JT. Post-sphincterotomy bleeding after the introduction of microprocessor-controlled electrosurgery: does the new technology make the difference?. *Gastrointestinal endoscopy*. 2005 Jan 1;61(1):53-7.
12. Tang Z, Yang Y, Yang Z, Meng W, Li X. Early precut sphincterotomy does not increase the risk of adverse events for patients with difficult biliary access: A systematic review of randomized clinical trials with meta-analysis and trial sequential analysis. *Medicine*. 2018 Sep;97(36).
13. Sundaralingam P, Masson P, Bourke MJ. Early precut sphincterotomy does not increase risk during endoscopic retrograde cholangiopancreatography in patients with difficult biliary access: a meta-analysis of randomized controlled trials. *Clinical Gastroenterology and Hepatology*. 2015 Oct 1;13(10):1722-9.
14. Manes G, Paspatis G, Aabakken L, Anderloni A, Arvanitakis M, Ah-Soune P, Barthet M, Domagk D, Dumonceau JM, Gigot JF, Hritz I. Endoscopic management of common bile duct stones: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy*. 2019 May;51(05):472-91.
15. Liu Y, Su P, Lin Y, Lin S, Xiao K, Chen P, An S, Bai Y, Zhi F. Endoscopic sphincterotomy plus balloon dilation versus endoscopic sphincterotomy

- for choledocholithiasis: A meta-analysis. *Journal of gastroenterology and hepatology*. 2013 Jun;28(6):937-45.
16. de Clemente Junior CC, Bernardo WM, Franzini TP, Luz GO, dos Santos ME, Cohen JM, de Moura DT, Marinho FR, Coronel M, Sakai P, de Moura EG. Comparison between endoscopic sphincterotomy vs endoscopic sphincterotomy associated with balloon dilation for removal of bile duct stones: A systematic review and meta-analysis based on randomized controlled trials. *World journal of gastrointestinal endoscopy*. 2018 Aug 16;10(8):130.
 17. Xu L, Kyaw MH, Tse YK, Lau JY. Endoscopic sphincterotomy with large balloon dilation versus endoscopic sphincterotomy for bile duct stones: a systematic review and meta-analysis. *BioMed research international*. 2015;2015.
 18. Jin PP, Cheng JF, Liu D, Mei M, Xu ZQ, Sun LM. Endoscopic papillary large balloon dilation vs endoscopic sphincterotomy for retrieval of common bile duct stones: a meta-analysis. *World Journal of Gastroenterology: WJG*. 2014 May 14;20(18):5548.
 19. Hwang JC, Kim JH, Lim SG, Kim SS, Shin SJ, Lee KM, Yoo BM. Endoscopic large-balloon dilation alone versus endoscopic sphincterotomy plus large-balloon dilation for the treatment of large bile duct stones. *BMC gastroenterology*. 2013 Dec;13(1):15.
 20. Lo SK. Bleeding from the Papilla. In Lee LS (ed). *ERCP and EUS. A Case-Based Approach*. Springer, New York, 2015, 263-276